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COD LIVER OIL: WHAT IS IT?

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Ever since 1841, when cod-liver oil was so strongly advocated by Bennett, it has held a prominent place in the confidence of physicians. From this date we find that many and careful studies have been made, so that we may say that its scientific use is of comparatively recent origin, although it has been employed empirically for nearly two hundred years. The chemistry of this subject is by no means, even now, complete, although many analyses have been made, so that at intervals one finds in the literature various hypotheses as to what ingredients this remedy's virtues may be attributed. In spite of discordant theories and the contradictory results of chemical analysis, cod liver oil is still regarded as a remedy of the highest value in diseases marked by malnutrition, of which pulmonary tuberculosis is the most frequent occasion for its employment.

What then can be said of its composition? Briefly, it is principally, first, olein glyceride (70 per cent.) with variable quantities of stearin, palmitin (nearly 25 per cent.), and myristin glycerides, the latter increasing with the darker color. So far no controversy has arisen beyond the unconfirmed statement of Winckler (1852) that glycerin could not be obtained from cod-liver oil, which he regarded as a whole, containing propyl oxide. Second, iodine, in from 0.0012 (Bird) to 0.004 per cent (De Jongh), its presence first demonstrated by De l'Orme, but even now it is not known in what form it exists. On the other hand, several observers have failed to detect it in all specimens. Third, bromine. Fourth, phosphorus: as pre-existent phosphoric acid, 0.0789; as obtained by total oxidation of the oil, 0.1047 per cent. (De Jongh). Fifth, sulphur. Sixth, biliary acids. Seventh, free acids, calculated as acetic acid, 0.01 to 1.80 per cent. (Charles, 1882), and regarded as butyric and acetic acids by De Jongh (1849). It is quite likely that free oleic, palmitic and stearic acids exist in the oil. Eighth, gaduin, $C_{35}H_{46}O_9$, identical with morrhuic acid (Gautier and Mourgues, 1888), existing as an unstable compound resembling lecithin, and in contact with acids and alkalies decomposing into morrhuic acid, $C_9H_{13}NO_3$, phosphoric acid and glycerin. Ninth, gadic acid (Luck, 1857), deposited from light-brown oil.

Under the name of morrhuolins are included the so-called alkaloids of cod-liver oil: morrhuic acid mentioned above; dihydrolutidin, $C_7H_{11}N$; asellin, $C_{25}H_{32}N_4$; amylamin, $C_5H_{13}N$; oxycollidin, $C_8H_{11}NO$; morrhuin, $C_9H_{27}N_3$; nicomorrhuin, $C_{20}H_{28}N_4$; the last four being the most active. Gautier and Mourgues found, however, in yellow oils six definite bases: butylamin, amylamin, hexylamin, dihydrolutidin, asellin, morrhuin, and morrhuic acid. It will be observed that they failed to find oxycollidin and nicomorrhuin. So far as the oily constituents, iodine, bromine, sulphur, phospho-

rus, biliary substances and free acids are concerned, there is virtual agreement in the results of analyses.

As to the so-called alkaloids, or definite bases, there is abundant opportunity for criticism. It is remarkable that they are most abundant in the brown oils, and from these is commercially obtained morrhuol, the name applied to an alcoholic extractive derivable from cod-liver oil and of probably indefinite chemical structure. Similarly the term "gaduol" has been employed. Presumably morrhuol, which according to Lafarge (1885) is a very aromatic substance of a sharp, bitter taste found in brown oils 4.50 to 6.00, yellow oils 2.50 to 3 00, and in white oils 1.50 to 2.00 per cent., contains most of the so-called alkaloids, together with the iodine, bromine, and phosphorus, and is the substance which is supposed to represent the active principles of the oil.

The physiological properties of the seven alkaloids have been determined by Gautier and Mourgues to be as follows:

Butylamin: In sufficient doses this produces in animals fatigue, stupor, vomiting and a certain degree of paresis. In small doses it excites the urinary secretions; in large doses it is at the same time convulsive and paralyzing; in medium doses it throws the animals into a sort of somnolence, with muscular paresis, but with complete conservation of the intelligence. Although poisonous, it does not produce death unless given in very large doses.

Amylamin: This is a very active base. In small doses it excites the reflexes and the urinary secretion. In large doses it provokes convulsive trembling, then regular convulsions and death.

Hexylamin acts almost like amylamin, but with less intensity.

Dihydrolutidin is a rather toxic base, even in small doses, when it produces a notable diminution of sensibility. In larger doses it provokes trembling and convulsions in the muscles of the face. With still larger doses in a guinea-pig the trembling increases and becomes more general. Very lively periods of excitation are followed by profound depression with insensibility and paralysis of the muscles, especially of the posterior members. The animal gradually goes into an asphyxiated collapse.

Asellin is only a feebly active base. In sufficient dose it produces dyspnœa, stupor, convulsive troubles, and in large doses death.

Morrhuin is one of the most active principles of the oil; it is also in larger quantity—a little more than one-third of the total alkaloids. This is believed to be a powerful stimulant to the function of nutrition and assimilation, producing a rapid circulation of the extractive residues of cell life towards the blood and kidneys, where they are eliminated, and in this way provoking indirectly a powerful movement of the assimilation. Virtually it is believed to increase the appetite and to provoke diaphoresis and diuresis.

As we read the results of these experiments, we cannot but be impressed by the fact that these symptoms are the symptoms of ptomaine poisoning. And when one remembers that the process of manufacturing hitherto employed is such that putrefaction is an important factor in the production of the oil, as anyone will testify who has visited the North Cape, where the stench encountered upon the journey is as prevalent and repulsive as that found near the menhaden-rendering works of the Atlantic Coast, the impression becomes a certainty. *Without doubt, the alkaloids contained in morrhuol are patrefactive or cadaveric alkaloids, and of these amylamin, asellin, dihydrolutidin are assuredly poisonous and are so classified in Gould's table as modified from Vaughan and Novy.* Amylamin can also be obtained from horn and from putrid yeast. Morrhuin, as is stated above, is probably diuretic and diaphoretic. Butylamin may or may not be toxic; it is quite probable the latter. *That any of these alkaloids are present in cod-liver oil when prepared at the place of the fisheries, by a proper process, is extremely doubtful.* So far as I can learn, no analyses have been made of such cod-liver oil. *To assume that morrhuol represents in any way the active therapeutic properties of cod-liver oil, is to assume that cod-liver oil is useful only in the pro-*

portion that it is putrefied. My attention having been called to the reports of Lafarge (1885), and later of Germain Sée, I experimented with morrhuol for several months, and finally, convinced of its absolute failure, I abandoned its use. I was so thoroughly positive of its uselessness that the paper of Bouillot did not induce me to repeat my observations. *If there are any medicinal properties in the preparations of the so-called active principles from which oil is removed, or which are removed from the oil, they must be entirely due to the other substances with which they are incorporated.* The substitution of active principles in place of crude drugs is praiseworthy, when it is proved that these active principles represent the properties of the drug or possess in themselves definite physiological action. No digitalin, or digitonin, or digitoxin, has yet been isolated which fully represents digitalis; why then need we expect that alkaloids shall represent cod-liver oil, even if they arise from its putrefaction?

To what then can we attribute the beneficial action of cod-liver oil in wasting diseases? *That cod-liver oil is a food, a food of special value, because of its peculiar properties.*

To quote Farquharson: "It has been proved by experiment that animal are more digestible than vegetable oils, and cod-liver oil is the most readily assimilated of all. After being emulsified by the pancreatic juice, it comes in contact with the bile, which distinctly increases its power in passing through moist animal membrane; and it is probable also that the biliary principles incorporated in its own structure aid in enabling it to be easily absorbed by the lacteals. Its action in the system is to improve the general constitutional tone, to evolve force and heat, and to aid in supplying those fatty elements which are so essentially requisite for the construction and repair of the tissues. It supplies the fatty matter on which the proper functions of cell growth and development depend, the nuclei of the cells being formed of fat."

The free fatty acids contained also aid in emulsification and absorption from the alimentary canal. It improves the nutrition and supplies the fatty ingredients necessary for the growth and repair of the nervous system. It improves the quality of the blood, increasing the number of the red corpuscles, and strengthens the heart muscle. Although the quantity of iodine, bromine and phosphorus is small, so far as their influence goes they are of use. Brunton has pointed out that, because it nourishes the young epithelial cells of the bronchial mucous membrane, enabling them to grow instead of being converted into pus, it is of undoubted efficacy as an expectorant.

Thousands of lives would undoubtedly have been saved, had the profession understood that beef tea, as formerly made, containing scarcely more than the soluble extractives, possesses about as much value as a nutrient as urine. Shall we now go on to administer the extractives of cod-liver oil, *cadaveric alkaloids of demonstrated poisonous properties*—of which the best that can be said is that one is diaphoretic and diuretic in its action and increases the appetite—and discard the really valuable constituents, which make up the food? A tuberculous patient can generate a sufficient amount of ptomaine without any assistance from the physician. It is the prevention of the formation, not elimination, that one seeks in treatment. An analogous procedure would be the administration of beef tea made from putrid meat.

The use of the extractives of cod-liver oil is no new idea. In 1866, an extract, an evaporated watery extract, made from the livers in preparing the oil, was used. It soon fell into disuse. Granting that the ptomaines of putrid oil are harmless—which is as yet by no means proven, for the quantity in which they have been administered has been too small for any definite conclusion—if there are any remedial properties in the extracts or wines it must be in the substances incorporated with them, but which are better administered separately.

How then shall we prescribe cod-liver oil? *By emulsions, which are heavily charged with*

mucilage and contain water which favors rancidity? Of all which I have used—and every one which I could obtain has been used in my hospital and dispensary service—but one has been satisfactory, and that only when freshly made. For fourteen years I have used an oil of which the only recommendation it claimed was that it was obtained from fresh livers by cold expression. It was of American origin, and on that account was not obtained from the cod when in as good condition as when off the shores of Norway. As it was, its use was far more satisfactory than that of emulsions or mixtures of whatever sort.

During the past few months I have used with great satisfaction the Improved Lofoten Cod-liver Oil made by Parke, Davis & Company, which is simply an oil obtained on the site of the fisheries from the livers of the fish at the time they are taken from the water. The process of manufacture is carefully carried out so that absolute cleanliness and freshness of the material shall be secured and that no decomposition shall take place. The disagreeable odor and flavor is removed, but no constituent important for its use as a food is taken out. Specimens kept for months have as yet shown no change. The problem seems to be solved. A food to be of its highest usefulness must be palatable; the most weighty objection is now done away with.

The oil should be given during the height of pancreatic digestion, one to two hours after eating, so that it may pass rapidly through the stomach and be absorbed during intestinal digestion. The stools should be watched that more shall not be administered than can be absorbed. If the oil should "repeat," a fact which I have not as yet observed, a few drops of ether added to the dose is likely to obviate that difficulty. The dose is from one to six teaspoonfuls. My conclusions are:

1. Cod-liver oil is a food, important because of its peculiar properties.

2. *Since it is a food, no extractive can represent its value.*

3. *The purer the oil—the more free from cadaveric alkaloids—the more palatable will it be and the better adopted for its purpose.*

4. The best that can be said of the cadaveric alkaloids is that they may possibly represent its eliminative, they certainly do not represent its reconstructive, properties.

5. It is not proven that the administration of appreciable quantities of the cadaveric alkaloids is devoid of danger.

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